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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/486,882	03/02/2000	DUNCAN MCGREGOR	1015-00	3081

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EXAMINER	
PONNALURI, PADMASHRI	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 11/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/486,882	MCGREGOR, DUNCAN	
	Examiner	Art Unit	
	Padmashri Ponnaluri	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-9 and 24-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-9, 24-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment and response filed on 9/12/05 has been fully considered and entered into the application.

2. Claim 10 has been canceled, and new claim 26 has been added by the amendment filed on 9/12/05.

3. Claims 1, 3-10 and 24-26 are currently pending in this application.

Priority

4. This application is a 371 of PCT/GB98/02630, which claims priority to a UK Application 9718455.

5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Specification

6. The substitute specification filed on 9/12/05 has been fully considered and entered into the application.

Withdrawn Claim Rejection

7. The indefiniteness rejection of claim 6 has been withdrawn.

Maintained Claim Rejections

8. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. The rejection of claims 1, 24 and 25 as being indefinite for the reasons set forth in the previous office action mailed on 5/11/05 has been maintained.

10. The rejection of claims 1, 3-6, 8-10 and 25 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent 5,498,530 (Schatz et al)

11. The rejection of claims 1, 3-10 and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,498,530 (Schatz et al) and US Patent 6,451,527 B1 (Larocca et al), is maintained for the reasons set forth in the previous office action.

Response to Arguments

12. Claims 1-10, 24-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 24, 25 recite that the 'chimeric protein-encoding portion of the recombinant polynucleotide is protected by a binding moiety which is a protein..', which is vague and indefinite, because it is not clear does applicants mean that the recombinant polynucleotide which is not bound by the DNA binding proteins is linked to a protein or covered by a protein. It is not clear what does applicants mean by protected by.

13. Applicant's arguments filed on 9/12/05, regarding the indefiniteness rejection of claims, have been fully considered but they are not persuasive.

Applicants argue that the claims have been amended to specify that 'the chimeric protein-encoding portion of the recombinant polynucleotide is protected from degradation by a binding moiety that binds non-specifically to the polynucleotide irrespective of nucleotide sequence.' Applicants assert that with the amendment that the examiner's objection has overcome.

Applicants amendment to the claims, and assertions have been fully considered

and are not persuasive. Because the instant the claim does not recite that the 'chimeric protein encoding portion is bound by the nucleotide binding portion.' Note in the instant claimed synthetic construct has a chimeric protein, and a recombinant polynucleotide, and further the chimeric protein has a nucleotide binding portion which binds the nucleotide sequence motif of the recombinant polynucleotide. The claim does not recite that the chimeric-protein encoding portion of the recombinant polynucleotide is bound by the nucleotide binding portion of the chimeric protein.

And further the claims are drawn to a product (a synthetic construct), and the limitation (the chimeric protein-encoding portion of the recombinant polynucleotide is protected from degradation by a binding moiety that binds non-specifically to the polynucleotide irrespective of nucleotide sequence) is considered as a process limitation.

Thus, for the reasons of record the rejection of record has been maintained.

14. Claims 1, 3-6, 8-10 and 25 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over US Patent 5,498,530 (Schatz et al).

The instant claims briefly recite a synthetic construct comprising a complex of a recombinant polynucleotide and a chimeric protein, wherein the chimeric protein has a) a nucleotide binding portion, which comprises a binding domain of a nuclear steroid receptor; and b) a target peptide portion, and said recombinant polynucleotide comprises a) a chimeric protein encoding portion which encodes the chimeric protein of the complex; and b) a nucleotide sequence motif which is specifically bound by the nucleotide binding portion of the chimeric protein, and the chimeric protein encoding portion of the polynucleotide is not bound by the chimeric protein, and is protected by a binding protein, which is able to bind non-specifically to polynucleotides.

NOTE the recitation 'for use as a peptide display carrier package' is considered as intended use, and Claim 10 limitations are considered as product-by-process limitations.

Schatz et al teach peptide libraries and screening. The reference teaches methods of generating peptide library, the method comprises a) constructing a recombinant DNA vector that encoded DNA binding protein and contains a binding site for the DNA binding protein (refers to the recombinant polynucleoitdes of the instant claims); and the vector encodes a fusion protein composed of DNA binding protein and the peptide (refers to the target) (chimeric protein of the instant claims). And the reference teaches that during the screening methods, the fusion proteins remain bound to the vector that encodes the fusion protein (refers to the instant claim recombinant polynucleotide and chimeric protein complex) (for example, see column 2). The reference teaches the use of different DNA binding proteins (for example, see column 6), which includes nuclear hormone receptor-type proteins, and the reference preferentially uses lac repressor as the DNA binding protein. At some point during the growth of the transformants, the fusion protein will be expressed, and because of the random peptide also contains DNA binding sites for DNA binding proteins, fusion proteins will bind to the vectors that encode them to form a complex (i.e., see column 11). The reference teaches that the DNA of the vector contain one or random peptide coding sequence and spacer (i.e., see column 8) (refers to instant claim 5). Further the reference teaches that the lac repressor fusion proteins of the present invention include not only carboxy terminus fusion but also amino terminus fusions (i.e., see column 7) (refers to instant claim 9).

The reference does not specifically teach the complex of chimeric protein comprising nuclear steroid receptor as DNA binding proteins. However, it would have been obvious to one skilled in the art at the time the invention was made to use the steroid receptor domains as DNA binding portion of the instant claims, because Schatz et al teach the advantages of the use of DNA binding moieties in phage vector screening, and teaches that the nuclear hormone receptors proteins as DNA binding proteins. The claimed invention differs from the prior art teachings by reciting that the chimeric encoding portion of

the recombinant polynucleotide is protected by a protein. Schatz et al teach recombinant polynucleotide and a chimeric protein complex. Schatz et al do not teach chimeric protein encoding portion of the polynucleotide is protected by a protein.

The claimed synthetic construct comprising a complex of a recombinant polynucleotide and a chimeric protein, appears to be the same or obvious variations of the reference teachings, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to determine and/or compare whether the chimeric encoding portion of the polynucleotide is protected by a protein (which is coat protein of the phage). The reference teaches the use of bacteriophage as the vector, same as the instant invention, and further the reference complex has all the components of the invention, thus the reference vectors are considered same as the instant claim vectors, thus the chimeric protein encoding portion is considered as protected by coat protein. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed synthetic construct (vector) is different from the one taught by prior art and to establish the patentable differences. See in re Best 562F.2d 1252, 195 U. S. P. Q. 430 (CCPA 1977) and Ex parte Gray 10 USPQ2d 1922(PTO Bedpan. App. & Int. 1989).

15. Applicant's arguments filed on 9/12/05, regarding the rejection of claims over Schatz et al, have been fully considered but they are not persuasive.

Applicants traverse the rejection. Applicants argue that the claim 1 has been amended to include 'construct is produced in a host cell transformed with said recombinant polynucleotide and extruded therefrom without lysis of the host cell.'

NOTE the amendment to the claims 'wherein said construct is produced in a host cell transformed with said recombinant polynucleotide and extruded therefrom without lysis of the host cell' is considered as product-by-process limitation.

Applicants argue that none of these features are taught or suggested by Schatz et al.

Applicant's arguments have been fully considered and are not persuasive. The limitations which are newly added are process limitations.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

In the present case, Schatz et al teach 'recombinant vectors that encode DNA binding protein and contains a binding site for the DNA binding protein and the vector encodes a fusion protein composed of DNA binding protein and the peptide , and during the screening methods, the fusion proteins remain bound to the vector that encodes the fusion protein and bind to the receptor', which reads on the instant claim synthetic construct. Schatz et al teaches that the recombinant polynucleotide is extracted by lysis of host cell, however the instant claim is not drawn to the process, and the vectors (product) of the reference read on the instant claimed vectors, even though it is made of a different process.

Applicants arguments regarding the 'methodology of Schatz is limited to peptides that are functionally folded in the cytoplasm and this limitation would reduce the range of suitable peptides considerably.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., Schatz is limited to peptides that are functionally folded in the cytoplasm) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the

specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants further argue that the methodology of Schatz et al inevitably results in a build up of potentially toxic proteins within the host cell; and Schatz et al fail to take account of the inherent inefficiencies of the system.

In response to applicant's argument that 'the methodology of Schatz et al inevitably results in a build up of potentially toxic proteins within the host cell; and Schatz et al fail to take account of the inherent inefficiencies of the system.' the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985).

Applicants further argue that in the Schatz et al reference the 'chimeric protein encoding portion is not protected by coat protein.' Applicants argue that the methodology of Schatz et al described in the exemplification uses plasmid vector pMC5 and figure 2 clearly lacks a gene encoding for the functional viral coat protein.

Applicant's arguments have been fully considered and are not persuasive. Since the instant claims are drawn to a product, and the claim limitations is considered as process limitation; further Schatz et al teach the use of recombinant DNA vectors which would includes a phage (i.e., see column 4); and further Schatz et al teach that the use of both phage and plasmid fusions increases the total available peptide diversity (i.e., see column 21).

Applicants arguments that 'Schatz et al totally fails to teach formation of a PDCP not that the target peptide may be expressed externally on such PDCP, and host cell lysis is essential in the Schatz methodology for harvest of the construct' have been fully considered and are not persuasive.

Applicant's arguments are not persuasive, in view of the Schatz et al teaching recombinant vectors that encode chimeric protein composed of DNA binding protein and the target peptide. And the limitation that 'the host cell lysis is essential in the Schatz methodology for harvest of the construct' is considered as intended use limitation and/or as a purpose of the process. And further the limitation is not a structural feature of the claimed product.

New claim 26 has been included in this rejection because the limitation 'the chimeric protein encoding portion of the recombinant polynucleotide is protected from degradation by a protein binding moiety,' and the 'binding moiety is a bacteriophage coat protein' is considered as process limitation. The instant claim is drawn to a product, thus the process limitation was not given the patentable weight.

Thus for the reasons of record the rejections have been maintained.

16. *Claims 1, 3-10 and 24-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,498,530 (Schatz et al) and US Patent 6,451,527 B1 (Larocca et al).*

The instant claims briefly recite a synthetic construct comprising a complex of a recombinant polynucleotide and a chimeric protein, wherein the chimeric protein has a) a nucleotide binding portion, which comprises a binding domain of a nuclear steroid receptor; and b) a target peptide portion, and said recombinant polynucleotide comprises a) a chimeric protein encoding portion which encodes the chimeric protein of the complex; and b) a nucleotide sequence motif which is specifically bound by the nucleotide binding portion of the chimeric protein, and the chimeric protein encoding portion of the polynucleotide is not bound by the chimeric protein, and is protected by a binding protein, which is able to bind non-specifically to polynucleotides.

NOTE the recitation 'for use as a peptide display carrier package' is considered as intended use, and claim 10 is considered as product-by-process limitation.

Schatz et al teach peptide libraries and screening. The reference teaches methods of generating peptide library, the method comprises a) constructing a recombinant DNA vector that encoded DNA binding protein and contains a binding site for the DNA binding protein (refers to the recombinant polynucleoitdes of the instant claims); and the vector encodes a fusion protein composed of DNA binding protein and the peptide (refers to the target) (chimeric protein of the instant claims). And the reference teaches that during the screening methods, the fusion proteins remain bound to the vector that encodes the fusion protein (refers to the instant claim recombinant polynucleotide and chimeric protein complex) (for example, see column 2). The reference teaches the use of different DNA binding proteins (for example, see column 6), which includes nuclear hormone receptor-type proteins, and the reference preferentially uses lac repressor as the DNA binding protein. At some point during the growth of the transformants, the fusion protein will be expressed, and because of the random peptide also contains DNA binding sites for DNA binding proteins, fusion proteins will bind to the vectors that encode them to form a complex (i.e., see column 11). The reference teaches that the DNA of the vector contain one or random peptide coding sequence and spacer (i.e., see column 8) (refers to instant claim 5). Further the reference teaches that the lac repressor fusion proteins of the present invention include not only carboxy terminus fusion but also amino terminus fusions (i.e., see column 7) (refers to instant claim 9).

The reference do not specifically teach the complex of chimeric protein comprising nuclear steroid receptor as DNA binding proteins, and reciting that the chimeric encoding portion of the recombinant polynucleotide is protected by a protein. Larocca et al teach genetic package display system for selecting internalized ligands. The reference teaches that in an

alternative embodiment, recovery of replicated internalized nucleic acid molecules may be achieved via a nucleic acid binding domain. Accordingly, when using phage, the phage genome can be altered such that a DNA binding sequence is incorporated therein. The phage may contain one or more copies of lac operon (i.e., see column 14). The reference teaches that a variety of nucleic acid binding proteins can be used in the claimed method, because of their sequence specific recognition. Host transcription factors have been grouped into seven well-established classes based upon the structural motif used for recognition. The major families include helix-turn-helix (HLH) proteins, homeodomains, zinc finger proteins, steroid receptors, leucine zipper proteins, helix-loop-helix(HLH) proteins, and P-sheets (refers to the steroid receptor of the instant claims) (i.e., see column 14). The reference further teaches steroid receptor proteins include receptors for steroid hormones, retinoids, vitamin D, thyroid hormones as well as other compounds. Specific examples include retinoic acid, kniprs, progesterone, androgen, glucosteroid and estrogen receptor proteins (i.e., see column 15). Thus, it would have been obvious to one skilled in the art at the time the invention was made to use different steroid receptors as DNA binding proteins in phage vector systems, because Larocca et al and Schatz et al teach the advantages of the use of DNA binding proteins in screening the phage vectors. And a person skilled in the art would have been motivated to use the steroid receptor proteins as DNA binding proteins, because the methods provide peptides with free carboxy or amino terminus, and add diversity in the structure for receptor binding.

17. Applicant's arguments filed on 9/12/05, regarding the rejection of claims over Schatz et al, have been fully considered but they are not persuasive.

Applicants argue that Larocca never suggested that the gene encoding for the protein binding partner is inserted in the phage genome, nor expressed therefrom. Thus, neither Larocca nor Schatz teach the production of a PDCP, which is the subject of the application in suit.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In this case the rejection was based on combined teachings of Schatz et al and Larocca et al. Schatz et al teach the use of different DNA binding proteins, including nuclear hormone receptor type proteins, and Larocca et al teach the use of altering the phage genome by incorporating DNA binding proteins. Thus, it would have been obvious to one skilled in the art to use steroid receptor proteins in the phage vector system.

New claim 26 has been included in this rejection because the limitation 'the chimeric protein encoding portion of the recombinant polynucleotide is protected from degradation by a protein binding moiety,' and the 'binding moiety is a bacteriophage coat protein' is considered as process limitation. The instant claim is drawn to a product, thus the process limitation was not given the patentable weight.

"[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." In re Thorpe, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)

And for the reasons set forth in the previous office action the rejection has been maintained.

Conclusion

18. No claims are allowed.

19. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Padmashri Ponnaluri whose telephone number is 571-272-0809. The examiner can normally be reached on Monday through Friday between 7 AM and 3.30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Padmashri Ponnaluri
Primary Examiner
Art Unit 1639

PADMASHRI PONNALURI
PRIMARY EXAMINER

18 November 2005